

## **AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions, and listings, of claims in the application:

### **Listing of claims:**

Please cancel claim 4 without prejudice, amend claims 1, 3 and 5-11, and add new claims 13-23 as follows:

1. (currently amended) A method of screening genes which comprises performing *in situ* hybridization of a tissue or cell sample of an organism, using a probe which hybridizes specifically with mRNA and/or expression sequence tag being a produce of gene expression, and examining the localization of the mRNA and/or expression sequence tag in the tissue or cell, wherein the function of the gene and/or expression sequence tag is unknown, and wherein the expression level of the mRNA and/or expression sequence tag changes in response to the event.
2. (original) The method according to claim 1, wherein the mRNA and/or the expression sequence tag being a product of gene expression, is expressing in cultured cells or tissue.
3. (currently amended) The method according to claim 1 ~~or 2~~, wherein the mRNA and/or the expression sequence tag being a product of gene expression is confirmed with a DNA chip or DNA microarray such as high-density oligonucleotide array.
4. (canceled)
5. (currently amended) The method according to ~~any one of claims 1 to 4~~ claim 1, wherein the gene and/or expression sequence tag has been cloned ~~but function of which is unknown.~~
6. (currently amended) The method according to ~~any one of claims 1 to 5~~ claim 1, wherein localization of at least two types of different mRNA or expression sequence tag is examined in one type of tissue or cell in a single screening.
7. (currently amended) The method according to ~~any one of claims 1 to 5~~ claim 1, wherein localization of one type of mRNA or expression sequence tag is examined in at least

two types of different tissue or cell in a single screening.

8. (currently amended) The method according to ~~any one of claims 1 to 7~~ claim 1 used for screening of a gene encoding a substance effective as a drug.

9. (currently amended) The method according to ~~any one of claims 1 to 7~~ claim 1 used for screening of a gene related to a disease.

10. (currently amended) The method according to ~~any one of claims 1 to 7~~ claim 1 used for examining the function of a gene or expression sequence tag that has been cloned but which is of unknown function.

11. (currently amended) A method of ~~monitoring gene expression~~ screening a gene and estimating a function of the gene which comprises collecting a tissue or cell sample from an organism each before occurrence, and after occurrence of an event, performing in situ hybridization in respect of each sample using a probe that specifically hybridizes with mRNA and/or an expression sequence tag being a product of gene expression, and examining changes in localization of the mRNA and/or expression sequence tag in the tissue or cell, wherein the function of the gene and/or expression sequence tag is unknown before screening, and wherein the expression level of the mRNA and/or expression sequence tag changes in response to an event.

12. (original) The method according to claim 11 wherein a tissue or cell sample is collected from an organism at at least 2 different points in time after occurrence of an event.

13. (new) A method of screening to identify a gene as a target for drug development, which comprises:

- (a) examining the expression of an mRNA and/or expression sequence tag being a product of gene expression before and after an event,
- (b) determining those mRNA and/or expression sequence tags whose expression has changed in response to the event,
- (c) designing a probe that will specifically hybridize with the mRNA and/or expression sequence tag whose expression has changed in response to the event,
- (d) performing *in situ* hybridization of a tissue or cell sample of an organism

- before and after the event by using the probe designed in step (c),
- (e) examining the localization of the mRNA and/or expression sequence tag in the tissue or cell before and after the event,
  - (f) determining those mRNA and/or expression sequence tags whose localization has changed in response to the event, and
  - (g) identifying those mRNA and/or expression sequence tags whose expression and localization have both changed in response to the event as targets for drug development,

wherein the function of the gene and/or expression sequence tag is unknown before screening.

14. (new) The method according to claim 13, wherein the mRNA and/or expression sequence tag is expressed in cultured cells or tissue.

15. (new) The method according to claim 13, wherein the expression of the mRNA and/or the expression sequence tag is confirmed with a DNA chip or DNA microarray such as high-density oligonucleotide array.

16. (new) The method according to claim 13, wherein the gene and/or expression sequence tag has been cloned.

17. (new) The method according to claim 13, wherein localization and expression of at least two types of different mRNAs and/or expression sequence tags are determined in one type of tissue or cell in a single screening.

18. (new) The method according to claim 13, wherein localization and expression of one type of mRNA and/or expression sequence tag are determined in at least two types of different tissues or cells in a single screening.

19. (new) The method according to claim 13, wherein the gene encodes a substance effective as a drug.

20. (new) The method according to claim 13, wherein the gene is related to a disease.

21. (new) The method according to claim 13 further comprising the step of determining

the function of the gene.

22. (new) The method according to claim 13, wherein the tissue or cell sample is collected from an organism at two or more different points in time after occurrence of an event.

23. (new) The method according to claim 13 or 21, wherein the event is ischemia or cancer.